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# Neurologic Anomalies of Perrault Syndrome

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**We report on an 18-year-old man with neurosensory hearing loss and his sister with neurosensory hearing loss, ovarian dysgenesis, mental retardation, generalized ataxia of the trunk and limbs, and saccadic dysmetria. A CT scan showed cerebellar hypoplasia. The cardinal manifestations of Perrault syndrome in females are neurosensory hearing loss and ovarian dysgenesis. Other anomalies, including neurologic and skeletal, have been reported in other individuals with Perrault syndrome. We review the neurologic anomalies in previous patients with Perrault syndrome. Neurologic data are available on 14 of 21 girls; 7 of 14 had neurologic abnormalities. The high incidence of neurologic anomalies suggest that ataxia or mental retardation may not be just coincidental findings, but pleiotropic manifestations of Perrault syndrome.**


**KEY WORDS: Perrault syndrome, cerebellar hypoplasia, ataxia, mental retardation**

## INTRODUCTION

Perrault syndrome is an autosomal recessive disorder characterized by gonadal dysgenesis and neurosensory hearing loss in females but only isolated neurosensory hearing loss in brothers. Perrault [1951] first documented the association of neurosensory deafness and ovarian dysgenesis in sisters. Since that time only 9 additional families with 25 affected individuals have been described [Christakos et al., 1969; Perez-Ballester et al., 1970; Pallister and Opitz, 1979; Granat et al., 1979; Bosze et al., 1983; McCarthy and Opitz, 1985; Nishi et al., 1988; Crux et al., 1992; Linssen et al., 1994]. Other anomalies, particularly neurologic and skeletal, have been observed sporadically. There is uncertainty whether these anomalies are coincidental findings or phenotypic expressions of the syndrome. Recently Linssen et al. [1994] presented three sibs (one female and two males) with Perrault syndrome who also all had neurologic abnormalities.

We have observed a brother and sister with Perrault syndrome. We describe the sister's CT brain findings and correlate them with her neurologic abnormalities and review the neurologic anomalies of Perrault syndrome.

## CLINICAL REPORTS

The proposita was seen first seen at age 16 8/12 years for lack of pubertal development. She was a term infant born normally with birthweight was 2,300 g and length of 50.8 cm. There were no neonatal complications. She was delayed in motor development and began physical therapy at age 1 year. She sat at 18 months and did not walk until 3½ years. Severe bilateral neurosensory hearing loss was diagnosed at age 18 months. A CT scan of the head and temporal bones showed a large cerebral spinal fluid collection infratentorially in the posterior inferior portion of the posterior fossa extending around the cerebellum, compatible with cerebellar hypoplasia. The petrous bones and the remainder of the brain were normal. At age 6 years she failed a school vision screen and subsequently was diagnosed with strabismus, hyperopia, and astigmatism. She has mildly impaired cognitive functioning. Her Performance Scale I.Q. was 70 (using deaf norms) at age 15 years. Throughout schooling she has received speech and occupational therapy.

At 16 8/12 years her height was 153.3 cm (7th centile) and weight was 42.2 kg (<5th centile). She had Tanner stage I breast and Tanner stage II pubic hair development. Genitalia were normal. She did not have any neurocutaneous sign or minor anomalies. Cranial nerves II–XII were intact including fundi except for mildly pale optic nerves. Eye movements showed somewhat jerky saccades. On motor exam she had normal strength, tone, bulk and symmetry. Coordination was abnormal showing finger to nose dysmetria bilaterally as well as bilateral intention tremor in the upper limbs. Heel to shin movement was mildly dysmetric. She was unable to stand on one foot for more than two seconds. She was unable to perform tandem gait and her ordinary gait was wide based and jerky. Rapid alternating movements were performed well, but with abnormal

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prosody. Her speech was not dysarthric. Deep tendon reflexes were +1 in the upper limbs , +2 in the lower limbs; there was no Babinski sign. Sensory status was intact to touch and joint position sense. The CT findings of hemisphere and vermis hypoplasia correlate with generalized ataxia of the limbs and trunk and saccadic dysmetria.

Laboratory evaluations showed LH = 33.7 mIU/mL (normal range <3.6–29.4 mIU/mL), FSH = 130.9 mIU/mL (normal range 2.8–17.2 mIU/mL), prolactin = 15.8 ng/mL (normal range 0–20 ng/mL), T4 = 6.5 mcg/mL (normal range 4.5–12.0 mcg/mL), and TSH = 3.5 mIU/mL (normal range 0.45–3.6 mIU/mL). Chromosomes were normal 46,XX. Her bone age was equivalent to 12 years. A pelvic ultrasound study demonstrated prepubertal size uterus measuring 5 × 1.2 × 1.8 cm; ovaries could not be identified.

The proposita's brother was 18 years old. He was a term infant born normally. Birth weight was 3,900 g and length was 55.9 cm. Bilateral severe neurosensory hearing loss was diagnosed at age 2 years. At age 8 years he was noted to have slight hyperopia and astigmatism without amblyopia nor strabismus. Cognitive skills were average. He attended hearing-impaired programs throughout his school years and was mainstreamed in high school. Pubertal development began at age 11 years. CT scan of the head at age 17 years was normal.

On examination his height was 193 cm (>95%) and weight 91 kg (90%). Genital development was at Tanner stage V. Cranial nerves II–XII were intact including fundi; his optic nerves were mildly pale. He had normal strength, muscle tone, bulk, and symmetry. Coordination was intact by finger to nose, heel to shin, tandem gait, and rapid alternating movements. He was able to stand on one foot for more than 5 seconds. His gait was normal. Deep tendon reflexes were +1 in the upper and +2 in the lower limbs. Touch and proprioception senses were normal. There was no Babinski sign.

## DISCUSSION

Including the above cases, 28 persons (22 females and 6 males) from 11 families with Perrault syndrome have been reported (Table I). The proposita in each family was a female with gonadal dysgenesis and severe neurosensory hearing loss. These two signs currently define the syndrome. In general the brothers, except the brothers in family X, have only neurosensory deafness. However, the females are more likely to have other anomalies. Abnormal neurologic findings are the most commonly reported anomalies, present in eight patients. Unfortunately, the correct frequency of neurologic abnormalities can not be ascertained since several previous reports were limited and did not include a description of either a normal or abnormal neurologic examination.

TABLE I. Neurologic Findings in Patients With Perrault Syndrome

| | | Cases | | |
|---|---|---|---|---|
| Author | Family | Sex | Ages | Neurologic findings |
| Perault et al. [1951] | I | F | 24 | Normal |
| | | F | 16 | Normal |
| Christakos et al. [1969] | II | F | 19 | Mental retardation |
| | | F | 16 | Mental retardation |
| | | F | 15 | Mental retardation |
| | | M | 19 | Not described |
| Perez-Ballester et al. [1970] | III | F | 28 | Not described |
| | | F | 17 | Not described |
| | | F | 14 | Not described |
| Pallister and Opitz [1979] | IV | F | 37 | Normal |
| | | M | 36 | Normal |
| | | M | 32 | Normal |
| | | F | 28 | Normal |
| | | F | 13 | Normal |
| Granat et al. [1979] | V | F | 17 | Not described |
| Bosze et al. [1983] | VI | F | 20 | Not described |
| | | F | 18 | Normal |
| McCarth, and Opitz [1985] | VII | F | 16 | Spastic diplegia, weakness lower Limbs, abnormal extraocular muscle movement |
| | | F | 4 | Normal |
| Nishi et al. [1988] | VII | F | 16 | Ataxia, nystagmus, abnormal extraocular muscle movement, weakness of lower limbs |
| | | F | 14 | Ataxia, nystagmus, abnormal extraocular muscle movement, weakness of lower limbs |
| Cruz et al., [1992] | IX | F | 26 | Not described |
| | | F | 34 | Not described |
| Linssen et al. [1994] | X | M | 31 | Dyspraxia, chorea, ataxia, hypotonia |
| | | M | 29 | Mental retardation, dyspraxia, chorea, ataxia, hypotonia |
| | | F | 27 | Mental retardation, ataxia, hypotonia |
| Gottschalk et al. [Present cases] | XI | M | 18 | Normal |
| | | F | 16 | Cerebellar hypoplasia, ataxia, saccadic dysmetria |

Neurologic abnormalities included mental retardation, ataxia, hypotonia/muscle weakness, limited extraocular muscle movement, chorea, and dyspraxia. Mental retardation was present in six individuals; three sisters in family II, a brother and sister in family X and our proposita. Ataxia was described in six persons: two sisters in family VIII, three sibs in family X, and our proposita. Hypotonia or muscle weakness of the lower limbs was also found in six persons, although the neurologic abnormalities present in the oldest sister in family VII was thought to be secondary to perinatal brain damage. There was no history of perinatal difficulties in the other five individuals. Three children had limited extraocular muscle movement. Chorea was described in two out of three sibs in family X. All the sibs in family X had a sensory neuropathy.

Cerebellar dysfunction appears to be a common finding in the Perrault syndrome. On CT imaging our patient had cerebellar hypoplasia which correlated with her neurologic findings. Skull CT imaging was also performed on three other patients with ataxia, two sisters in family VIII, and the youngest sister in family X. These studies were normal.

The question remains whether neurologic anomalies in patients with Perrault syndrome are coincidental findings or pleiotropic manifestation. In the first six families described with Perrault syndrome, only one report mentioned neurologic anomalies [Perrault et al. 1951; Christakos et al., 1969; Perez-Ballester et al., 1970; Pallister and Opitz, 1979; Granat et al., 1979; Bosze et al., 1983]. Since then five additional families have been identified and 7 of 11 individuals in those families had abnormal neurologic findings [McCarthy and Opitz, 1985, Nishi et al., 1988; Crux et al., 1992; Linssen et al., 1994]. Recent clinical observations seem to suggest that the phenotypic manifestations of Perrault syndrome are not limited to ovarian dysgenesis and neurosensory hearing loss.

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